

Amendments to the Specification:

Please replace the paragraph beginning at page 13, line 10, with the following amended paragraph:

As a simple example of the intensity ratio method, suppose a gene of interest (target) is an HIV protease gene with the sequence 5'-ATGTGGACAGTTGTA-3' (SEQ ID NO:1). Suppose further that a sample sequence is suspected to have the same sequence as the target sequence except for a mutation of base C to base T at the underlined base position. Although hundreds of probes may be synthesized on the chip, the complementary mutation probes synthesized to detect a mutation in the sample sequence at the suspected mutation position may be as follows:

3'-TATC
3'-TCTC
3'-TGTC (wild-type)
3'-TTTC

The mutation probe 3'-TGTC is also the wild-type probe as it should bind most strongly with the target sequence.

Please replace the paragraph beginning at page 14, line 10, with the following amended paragraph:

Initially, each mutation base intensity is reduced by the background or "blank" cell intensity. This is done as follows:

A -> 45 - 2 = 43
C -> 8 - 2 = 6
G -> 32 - 2 = 30
T -> 12 - 2 = 10

Then, the base intensities are sorted in descending order of intensity. The above bases would be sorted as follows:

A -> 43
G -> 30
T -> 10
C -> 6

Next, the highest intensity base is compared to the second highest intensity base. Thus, the ratio of the intensity of base A to the intensity of base G is calculated as follows: $A:G = 43 / 30 = 1.4$. The ratio A:G is then compared to a predetermined ratio cutoff, which is a number that specifies the ratio required to identify the unknown base. For example, if the ratio cutoff is 1.2, the ratio A:G is greater than the ratio cutoff ($1.4 > 1.2$) and the unknown base is called by the mutation probe containing the mutation A. As probes are complementary to the sample sequence, the sample sequence is called as having a mutation T, resulting in a called sample sequence of 5'-ATGTGGATAGTGTGTA-3' (SEQ ID NO:2).

Please replace the paragraph beginning at page 15, line 6, with the following amended paragraph:

The second highest intensity base is then compared to the third highest base. The ratio of A:G is 4. The ratio of A:G is then compared to the ratio cutoff of 1.2. As the ratio A:G is greater than the ratio cutoff ($4 > 1.2$), the unknown base is called by the mutation probes containing the mutations C or A. As probes are complementary to the sample sequence, the sample sequence is called as having either a mutation G or T, resulting in a sample sequence of 5'-ATGTGGAKAGTGTGTA-3' (SEQ ID NO:3) where K is the IUPAC code for G or T(U).

Please replace the paragraph beginning at page 18, line 23, with the following amended paragraph:

As a simple example of one implementation of the reference method, suppose a gene of interest (target) has the sequence 5'-AAAACTGAAAA-3' (SEQ ID NO:4). Suppose a reference sequence has the sequence 5'-AAAACCGAAAA-3' (SEQ ID NO:5), which differs from the target sequence by the underlined base. The reference sequence is marked and exposed to probes on a chip with the target sequence being the chip wild-type. Suppose further that a sample sequence is suspected to have the same sequence as the target sequence except for a mutation at the underlined base position in 5'-AAAACTGAAAA-3' (SEQ ID NO:4). The sample sequence is also marked and exposed to probes on a chip with the target sequence being the chip wild-type. After hybridization and scanning, the following probe intensities (not actual data) were found for the respective complementary probes:

Reference		Sample	
3'-TGAC	-> 12	3'-GACT	-> 11
3'-TGCC	-> 9	3'-GCCT	-> 30
3'-TGGC	-> 80	3'-GGCT	-> 60
3'-TGTC	-> 15	3'-GTCT	-> 6

Although each fluorescence intensity is from a probe, the probes may be identified by their unique mutation base so the bases may be said to have the following intensities:

Reference		Sample	
A	-> 12	A	-> 11
C	-> 9	C	-> 30
G	-> 80	G	-> 60
T	-> 15	T	-> 6

Thus, base A of the reference sequence will be described as having an intensity of 12, which corresponds to the intensity of the mutation probe with the mutation base A. The reference method will now be described as calling the unknown base in the sample sequence by using these intensities.

Please replace the paragraph beginning at page 24, line 26, with the following amended paragraph:

As a simple example of this implementation of the reference method, suppose a reference sequence has a sequence of 5'-AAACCCAATCCACATCA-3' (SEQ ID NO:6) and a sample sequence has a sequence of 5'-AAACCCAGTCCACATCA-3' (SEQ ID NO:7), where the mutant base is underlined. Thus, there is a mutation of A to G. Suppose further that the reference and sample sequences are tiled on chips with the reference sequence being the chip wild-type. This implementation of the reference method will be described as identifying this mutation base.

Please replace the paragraph beginning at page 24, line 35, with the following amended paragraph:

For illustration purposes, this implementation of the reference method is described as filling in a data table shown in Fig. 5B (SEQ ID NO:6, SEQ ID NO:28, SEQ ID NO:29). Although the data table contains more data than is required for this implementation, the portions

of the data table that are produced by steps in Fig. 5A are shown with the same reference numerals. The generation of a data table is not necessary, however, and is shown to aid the reader in understanding the method. The mutant base position is at position 241 in the reference and sample sequences, which is shown in bold in the data table.

Please replace the paragraph beginning at page 29, line 34, with the following amended paragraph:

As a simple example of the statistical method, suppose a gene of interest (target) has the sequence 5'-AAAACTGAAAA-3' (SEQ ID NO:4). Suppose a reference sequence has the sequence 5'-AAAACCGAAAA-3' (SEQ ID NO:5), which differs from the target sequence by the underlined base. Suppose further that a sample sequence is suspected to have the same sequence as the target sequence except for a T base mutation at the underlined base position in 5'-AAAACTGAAAA-3' (SEQ ID NO:4). Suppose that in multiple experiments the reference sequence is marked and exposed to probes on a chip. Suppose further the sample sequence is also marked and exposed to probes on a chip.

Please replace the paragraph beginning at page 37, line 5, with the following amended paragraph:

Fig. 8 illustrates the main screen and the associated pull down menus for comparative analysis and visualization of multiple experiments (SEQ ID NO:8 and SEQ ID NO:9). The windows shown are from an appropriately programmed Sun Workstation. However, the comparative analysis software may also be implemented on or ported to a personal computer, including IBM PCs and compatibles, or other workstation environments. A window 802 is shown having pull down menus for the following functions: File 804, Edit 806, View 808, Highlight 810, and Help 812.

Please replace the paragraph beginning at page 39, line 12, with the following amended paragraph:

Fig. 9 illustrates an intensity graph window for a selected base at position 120 (SEQ ID NO:30 and SEQ ID NO:31). The filename containing the sequence data is displayed at 904. The graph shows the intensities for each of the hybridized probes associated with a base. Each grouping of four vertical bars on the graph, which are labeled as "a", "c", "g", and "t" on line 906, shows the background subtracted intensities of probes having the indicated substitution base. In

one embodiment, the called bases are shown in red. The wild-type base is shown at line 908, the called base is shown at line 910, and the base position is shown at line 912. In Fig. 9, the base selected is at position 120, as shown by arrow 914. The wild-type base at this position is T; however, the called base is M which means the base is either A or C (amino). The user is able to use intensity graphs to visually compare the intensities of each of the possible calls.

Please replace the paragraph beginning at page 39, line 28, with the following amended paragraph:

Fig. 10 illustrates multiple intensity graph windows for selected bases (SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, and SEQ ID NO:35). There are three intensity graph windows 1002, 1004, and 1006 as shown. Each window may be associated with a different experiment, where the sequence analyzed in the experiment may be either a reference (if it has associated probe intensity data as in the chip wild-type) or a sample sequence. The windows are aligned and a rectangular box 1008 shows the selected bases' position in each of the sequences (position 162 in Fig. 10). The rectangular box aids the user in identifying the selected bases.

Please replace the paragraph beginning at page 40, line 27, with the following amended paragraph:

Fig. 11 illustrates the intensity ratio method correctly calling a mutation in solutions with varying concentrations (SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, and SEQ ID NO:18). A window 1102 is shown with a chip wild-type 1104 and a mutant sequence 1106. The mutant sequence differs from the chip wild-type at the position indicated by the rectangular box 1108. The chip wild-type and mutant sequences are a region of HIV Pol Gene spanning mutations occurring in AZT drug therapy.

Please replace the paragraph beginning at page 43, line 22, with the following amended paragraph:

Fig. 13 illustrates the output of the ViewSeq™ program with four pretreatment samples and four posttreatment samples (SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, and SEQ ID NO:27). Note the base change at position 207 where a mutation has arisen. Even adjacent two additional mutations (gt), the "a" mutation has been properly detected.